REMARKS

Reconsideration of the allowability of the present application in view of the foregoing amendments and following remarks is requested respectfully.

Status of the Claims

Claims 110-177 are canceled (claims 1-109 having been canceled previously), and new claims 178-257 are presented in the Listing of Claims set forth in this Reply. Accordingly, claims 178-257 are presently pending in the application.

Support for new claims 178-257 is found throughout the specification. Support for the independent claims is also found specifically as follows:

Independent Claims	Citation
178 and 211:	Page 8, lines 26-31; page 9, lines 24-26; page 10, lines 6-7, 11-12, 14-16, 18-23; and page 12, lines 25-30 (collectively, "Citation 1").
240 and 246:	Citation 1; page 5, lines 14-15, 18-23; page 9, line 4; page 9, line 23 to page 10, line 6; and page 12, lines 25-27.
252:	Citation 1; page 11, line 27 to page 12, line 17; page 13, lines 1-2.

Support for the dependent claims is found in the citations for the independent claim from which they depend and is also found specifically as follows:

Dependent Claims	Citation
179-181:	Page 11, lines 4-9 and 23-24.
182-186, 193-199, 207-209, 222-226, 229-231, 233-238, 241-245, 247-251:	Page 5, lines 14-15, 18-23; page 9, line 4;

	and page 9, line 23 to page 10, line 6.
Dependent Claims	Citation
187-188, 192, 227-228, 232, 210, 239:	Page 5, lines 15-16.
189-191:	Page 10, lines 4-5.
200, 203:	Page 11, lines 4-18.
201-202, 204, 213-214:	Page 13, lines 4-28, page 14, lines 20-24.
205-206:	Page 11, line 27 to page 12, line 17.
212:	Page 5, lines 26-32; page 12, lines 5-17.
215:	Page 14, lines 26-29.
216-221:	Page 15, lines 1-16.
253-257	amended claims 1, 39, 41, and 47 submitted with Reply dated 9/26/01

Remarks Concerning Rejections in Office Action

In view of applicants' cancellation of claims 110-177 as set forth in the above Listing of Claims, the rejections set forth in the Office Action have been rendered moot. Accordingly, applicants request respectfully that these rejections be withdrawn. Notwithstanding the mootness of the rejections of the now-canceled claims, applicants provide the following comments to assist the Examiner in appreciating the patentability of the presently-claimed invention in view of the references relied upon in rejecting the now-canceled claims.

Bachynsky

Claims 110-113, 118-131, 133, 134, 136-147, 152-164, 166, 167 and 169-177 were rejected under 35 U.S.C. § 102(b) as being anticipated by Bachynsky et al., Irish Patent No.

(11) 63119, and Bachynsky et al., U.S. Patent No. 5,190,748 (collectively, "Bachynsky"). According to the Examiner, Bachynsky teaches a process for providing a blend of a ceftriaxone and a salt of a medium chain fatty acid having a carbon chain length of from 6 to 20 carbon atoms, with optional constituents Laureth-12 and Witepsol™ H15. The Examiner further characterizes the blend of Bachynsky, as well as each constituent thereof, as solids at room temperature, and that the blend of Bachynsky is capable of being formed into oral dosage forms, including enterically coated dosage forms, in which the sodium caprylate serves as an enhancer.

As an initial matter, applicants wish to point out that, upon receipt of the previous Action, a partner of the undersigned conferred with a representative of the manufacturer of Laureth-12 and was advised that Laureth-12 is a solid at room temperature. The representative advised also that the MSDS, upon which applicants had relied in making its prior assertions concerning Laureth-12, erroneously describes the material as a liquid and that this was probably attributable to human error.

Apart from the physical state of Laureth-12 and whether applicants would otherwise agree with all aspects of the Examiner's characterization of Bachynsky, applicants' claims, nonetheless, distinguish over the disclosure of Bachynsky at least by requiring the medium chain fatty acid salt to be the ***only*** enhancer present in the claimed composition.

Bachynsky, as explained below, refers to the use of a ***two-component enhancer*** which is referred to us an "absorption enhancing system." More specifically, all absorption enhancing systems disclosed in Bachynsky are made up of a first component, which is an ether of a C6 to C18 alcohol and a polyethylene glycol, together with a second component selected from among: (1) polyoxyethylene glycol C6 to C18 glyceride esters; (2) C6 to C18 carboxylic acids or salts thereof; and (3) esters of two or more C6 to C18 carboxylic acids, glycerol and a polyoxyethylene glycol. *See* Bachynsky (US) at col. 2, lines 2-18. While Bachynsky identifies several suitable medium chain fatty acid salts, including sodium caprylate, ***all*** of the compositions and dosage forms taught in Bachynsky require the presence of ***at least two absorption enhancers***. As a result, ***all*** of the compositions and dosage forms of Bachynsky that include a medium chain fatty acid salt ***must also contain*** a second component in the absorption enhancing system and that component functions also as an absorption enhancer together with the medium chain fatty acid salt.

Accordingly, there are no compositions or dosage forms taught in or suggested by Bachynsky that contain a medium chain fatty acid salt as the sole enhancer, as recited in all of applicants' independent claims.

Fujii

Claims 110, 114, 116, 117, 119 and 176 were rejected under 35 U.S.C. § 102(b) as being anticipated by Fujii et al., U.S. Patent No. 5,840,685 ("Fujii"). All of applicants' claims distinguish over the disclosure of Fujii at least by requiring the medium chain fatty acid salt to be the only enhancer present in the claimed composition.

The only "Fujii" embodiment which contains but one enhancer (referred to by Fujii as an "absorption promoter") is a composition in which the enhancer is either an anionic or a nonionic surfactant; as regards this embodiment, there is absolutely no reference to a medium chain fatty acid salt, as recited in applicants' claims. The other Fujii embodiment discloses the use of a salt of a medium chain aliphatic carboxylic acid, but **in admixture** with another absorption promoter Fujii's description of the aforementioned embodiments, neither of which anticipates applicants' claims, is set forth below.

> The absorption promoters for use in the present invention may be selected from an anionic and/or nonionic surfactant and a combination type absorption promoter, e.g., a nonionic surfactant plus a medium chain aliphatic carboxylic acid and its salts.*See* Fujii at col. 5, lines 61-65.

Thus, while Fujii contemplates the use of either a single-component or a two-component absorption promoter, the ***only*** embodiments which employ a single-component absorption promoter are those in which an anionic or nonionic surfactant is used. ***All*** of the compositions and dosage forms of Fujii with an absorption promoter containing a medium chain fatty acid or salt thereof ***must also contain*** a nonionic surfactant as a second component.

Accordingly, there are no compositions or dosage forms taught in or suggested by Fujii that contain a medium chain fatty acid salt as the sole enhancer, as recited in all of applicants' independent claims.

Watts

Claims 110-131, 133, 134, 136-164, 166, 167, and 169-177 were rejected under 35 U.S.C. § 102(b) as being anticipated by Watts et al., WO 97/05903 ("Watts"). Each of applicants' present claims distinguishes over the Watts disclosure in reciting that the medium chain fatty acid salt is the only enhancer present in the composition. Accordingly, the aforementioned section 102 rejection does not apply to the present claims.

Watts discloses unambiguously and definitively the use of a ***two-component*** absorption promoter as follows.

> The present invention therefore provides a drug delivery composition for colonic delivery comprising a polar drug, an absorption promoter which (a) comprises **a mixture** of a fatty acid having 6 to 16 carbon atoms or a salt thereof ***and a dispersing agent*** or (b) comprises **a mixture** of mono/diglycerides of medium chain fatty acids ***and a dispersing agent*** and means adapted to release the polar drug and absorption promoter in the colon. Watts at page 5, lines 10-16 (emphasis supplied).

Both of the Watts embodiments describe the absorption promoter as a **two-component mixture** in which one component must be a dispersing agent while the other may be either: (1) a medium chain fatty acid or salt; or (2) a mixture of mono/diglycerides of medium chain fatty acids. While additional details are provided as to particular fatty acids and salts, mono and diglycerides, and dispersing agents that are suitable in the practice of the Watts invention, the scope of Watts' invention extends ***only*** to the use of two-component absorption promoters. All of the embodiments which employ a medium chain fatty acid or salt thereof in the absorption promoter ***must also contain*** a dispersing agent as a second component of the absorption promoter. Accordingly, the Examiner's characterization of the Watts dispensing agent as being an "auxiliary excipent" is an incorrect, self-serving characterization.

There is additional information in the Watts disclosure that makes abundantly clear that what Watts is all about is a **two-component absorption promoter** and information which points directly away from the use of "one-component" absorption promoter, as set forth in applicants' claims. Thus, Watts discloses in Example 3 a composition in which

capric acid (not a salt of the acid) is used as the sole absorption promoter and this example is described as being a **comparative example**.

As shown below, the differences in the physical properties of capric acid as compared with its salt, such as its sodium salt, and the resultant properties of mixtures of each with an active ingredient are significant.

	Sodium caprate	Capric acid
Molecular Formula	$C_{10}H_{19}O_2Na$	$C_{10}H_{20}O_2$
Melting Point	240°C	31°C
Description	White to cream coloured powder	White crystals
Solubility	Soluble in water	Immiscible in water

As noted above, capric acid has a melting point of 31°C and is immiscible in water. Because its melting point is so close to room temperature, it is difficult to form a homogeneous particulate mixture of capric acid with an active ingredient having a sufficiently small particle size to be suitable for tableting or dry encapsulation. As taught in Watts, the capric acid is heated and the sodium insulin is added to the liquid and then cooled. The resulting composition would be a solitary mass of capric acid with sodium insulin mixed therein. By contrast, sodium caprate has a significantly higher melting point and is readily soluble in water so that a homogeneous particulate mixture of sodium caprate with an active ingredient that has a sufficiently small particle size to be suitable for tableting or dry encapsulation may be readily formed. As a result, the comparative example in Watts of a mixture of capric acid and sodium insulin is a disclosure quite unlike, and in no way suggestive of compositions and dosage forms comprising a drug and a medium chain fatty acid salt as the sole enhancer, as recited in all of applicants' independent claims.

Moreover, insofar as the insulin/capric acid mixture of the comparative example in Watts is considered inferior to mixtures utilizing a two-component absorption enhancer, Watts teaches away from using a medium chain fatty acid salt as the sole enhancer. Further, all of the compositions of Watts which include a medium chain fatty acid are disclosed in the

form of a suspension in liquid form or cooled to a semi-solid. There is no teaching or suggestion to provide such compositions in any other form, and in particular, in a compressible form.

Accordingly, there are no compositions or dosage forms taught or suggested by Watts that use a medium chain fatty acid salt as the sole enhancer, as recited in all of applicants' independent claims, and no compositions that are provided in compressible form, as recited in all of applicants' composition claims.

The Obviousness Rejections

The Examiner also rejected claims 110-134, 136-167, and 169-177 under 35 U.S.C. § 103(a) as being obvious over Watts in view U.S. Patent No. 6,017,559 ("Mulqueen") and also as being obvious over Watts in view of U.S. Patent No. 6,270,804 ("Getz"). Applicants note that Mulqueen and Getz were cited only with respect to certain dependent claims for their disclosures of elements recited in such dependent claims that are admittedly not found in Watts. Insofar as neither Mulqueen nor Getz cures the basic deficiencies of Watts as an anticipatory disclosure with respect to the independent claims, the combination of Mulqueen or Getz with Watts fails to teach or suggest the invention of the cited dependent claims as well.

Rejection of Macromolecular as Indefinite

The previously pending claims were also rejected as indefinite for reciting the term "macromolecular." While the claims that were rejected on this basis have been canceled, the claims set forth in the Listing of the Claims above use the term "macromolecular." Accordingly, applicants address the substance of the rejection in order to avoid its application to the pending claims.

The standard to be applied is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. *See* MPEP 2173.02. Claims should be allowed "which define the patentable subject matter with a reasonable degree of particularity and distinctness." *Id.* (emphasis in original). Thus, as explained in the MPEP, "definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

Id.

The term "macromolecular" is used in the specification to modify the "drug" and, read in context, would be reasonably clear to one of ordinary skill in the art. As set forth at page 9 of the specification:

> The term "drug" also explicitly includes those entities that are poorly absorbed via the oral route including hydrophilic drugs or ***macromolecular drugs*** such as peptides, proteins, oligosaccharides, polysaccharides or hormones including, but not limited to, insulin, calcitonin, calcitonin gene regulating protein, atrial natriuretic protein, colony stimulating factor, betaseron, erythropoietin (EPO), interferons, somatropin, somatotropin, somatostatin, insulin-like growth factor (somatomedins), luteinizing hormone releasing hormone (LHRH), tissue plasminogen activator (TPA), thyrotropin releasing hormone (TRH), growth hormone releasing hormone (GHRH), antidiuretic hormone (ADH) or vasopressin and analogues thereof such as for example desmopressin, parathyroid hormone (PTH), oxytocin, estradiol, growth hormones, leuprolide acetate, goserelin acetate, naferelin, buserelin, factor VIII, interleukins such as interleukin-2, and analogues thereof and anti-coagulant agents such as heparin, heparinoids, low molecular weight heparin, hirudin, and analogues thereof, bisphosphonates including alendronate and etidronate, pentassacharides including anticoagulent pentassacharides, antigens, adjuvants and the like.

See Specification at p. 9, line 24 to p. 10, line 6. In this context, the term "macromolecular" is used to describe a variety of compound classes including peptides, proteins, oligosaccharides, polysaccharides and hormones. In doing so, the commonly understood molecular weight ranges for these classes of compounds establish a reference by which one of ordinary skill in the art would understand the term "macromolecular." Moreover, the term "macromolecular drug" is found in over eighty issued U.S. patents and, according to a search recently performed on Google Scholar, in well over 600 scientific papers. As such, it is a term that would not be unfamiliar to a person of ordinary skill in the art and, viewed in the context of the specification, would define the patentable subject matter with a reasonable

degree of particularity and distinctness. As a result, applicants respectfully submit that the use of the term "macromolecular" in the pending claims should require no correction.

It is submitted also that the Examiner's comments as to why the term "macromolecular" is considered to be indefinite are not well taken. The "Hackh" definition (Exhibit A of applicants' Reply of September 14, 2006) states definitively that the chemistry of macromolecular molecules (for example, drugs herein) involve large and complex molecules whose molecular weight exceeds 1,000. This is a definitive definition unlike the "McGraw-Hill" definition which is general in nature. There is no information of record which is inconsistent with the "Hackh" definition and, accordingly, the claim term "macromolecular" is indeed definitive and in compliance with Section 112.

Conclusion

In view of the foregoing amendments and remarks, applicants respectfully submit that the Listing of the Claims set forth above places this case in condition for allowance. Accordingly, applicants respectfully request favorable consideration and early issuance of a Notice of Allowance. If the Examiner believes any issues remain, the undersigned requests a telephone interview prior to the issuance of an Action.

Respectfully submitted,

/Joshua R. Slavitt/
Joshua R. Slavitt
Reg. No. 40,816

Synnestvedt & Lechner LLP
2600 Aramark Tower
1101 Market Street
Philadelphia, PA 19107-2950
Telephone - (215) 923-4466
Facsimile - (215) 923-2189